





# MEA2100-System

**USER MANUAL** 

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# IMPRINT

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#### WELCOME TO THE MEA2100-SYSTEM



The MEA2100-System is the latest development in the MEA product family of Multi Channel System MCS GmbH. The MEA2100-System is a compact and portable stand-alone system for extracellular recordings from microelectrode arrays (MEAs) with integrated amplification, data acquisition, online signal processing, integrated stimulus generator as well as temperature control.

The MEA2100-System consists of two main devices: The interface board with integrated signal processor and the headstage equipped with amplifier, A / D converter and stimulus generator. It is possible to connect one headstage only or two headstages to one interface board. If you are dealing with two headstages, each headstage can be operated independently by opening the data acquisition software for each headstage separately.

It is a highly flexible system, using a headstage that will fit on inverted and upright microscopes. The MEA2100-System acquires data from up to 256 electrode channels and a sampling frequency of 50 kHz per channel. Up to eight additional analog in channels are available, and a 16 bit digital in / out channels. The digitized electrode data is transmitted to the connected interface board via iX-industrial cable. The connection between interface board and computer uses a super speed USB 3.0 connection. Thus, it is possible to use any computer as a data acquisition computer, also a laptop.

Data is recorded, stimulated, analyzed, graphed and reviewed with the powerful and easy-to-use Multi Channel Suite or MC\_Rack program from Multi Channel Systems MCS GmbH. The control functions of the internal stimulator are also integrated into both software. The data format can be converted in other standard formats with integrated software tools.

# The Headstage of the MEA2100-System

At the moment four different types of headstages are available for MEA2100-Systems. A headstage for microelectrode arrays (MEAs) with 256 electrodes, a headstage for microelectrode arrays with 120 electrodes, a headstage for microelectrode arrays with 60 electrodes or for two MEAs with 60 electrodes respectively and 12 stimulation electrodes.

The data acquisition integrated in the headstage supports 256 or 120 electrode channels. The sampling rate, signal range and bandwidth can be adjusted via software control and is suitable for a broad range of applications, from single unit spike recordings to field potentials from whole heart preparations.

A special advantage are the three integrated stimulus generator units, which deliver monophasic or biphasic rectangular pulses, as single pulses or pulse trains. You can choose between current or voltage stimulation and you can select each MEA electrode for stimulation within the software. The integrated blanking circuit (BC) disconnects the electrodes from the amplifiers during the stimulation and avoids stimulus artifacts.

As usual in MEA-Systems, the MEA2100-System features a heating element with a Pt100 temperature sensor. If you connect a temperature controller TC02 to the heating element via D-Sub 9 connector, the heating element guarantees constant temperature conditions for the biological sample on the chip. A perfusion system with heating is available for the MEA2100 as optional accessory.

All MEA types with 60 or 120 or 256 electrodes can be used. A modified base plate is available for the headstage to be able to work with perforated MEAs also.

Because of the compact designed headstage you can use most inverted or upright microscopes, for the optical control of the sample on the MEA chip.

# WELCOME TO THE MEA2100-SYSTEM

# The Interface Board of the MEA2100-System

The interface board of the system is equipped with a high-capacity digital signal processor DSP. By moving the detection and analysis of signals and from the data acquisition computer to the digital signal processor inside the interface, it is possible to run online filtering, analysis and feedback stimulation in real-time.

The digital in / out connector for 16 digital in- and output bits guarantees the communication with other devices. You can use the digital TTL inputs, for example, for synchronizing the recording in MEA2100-System with other systems. The digital TTL outputs can be used for triggering other devices, for example, an imaging setup.

Four digital inputs and four digital outputs (bit 0 to bit 3) are separately available via Lemo connectors on the front of the interface board. The up to eight analog inputs are intended for recording additional information from external devices, for example, for recording patch clamp in parallel to the MEA recording, for monitoring the temperature, or for fluidic control.

Two of the analog inputs are separately available via Lemo connectors on the front of the interface board. You can connect an audio system to the audio out connector to make electrical activity audible. This audio output is in real-time. Headphones or a speaker can be connected directly to the audio out. Two channels at a time can be converted into sound.

# IMPORTANT SAFETY ADVICE



Warning: Make sure to read the following advice prior to installation or use of the device and the software. If you do not fulfill all requirements stated below, this may lead to malfunctions or breakage of connected hardware, or even fatal injuries.



Warning: Always obey the rules of local regulations and laws. Only qualified personnel should be allowed to perform laboratory work. Work according to good laboratory practice to obtain best results and to minimize risks.

The product has been built to the state of the art and in accordance with recognized safety engineering rules. The device may only

- → be used for its intended purpose;
- → be used when in a perfect condition.

Improper use could lead to serious, even fatal injuries to the user or third parties and damage to the device itself or other material damage.



Warning: The device and the software are not intended for medical uses and must not be used on humans. MCS assumes no responsibility in any case of contravention.

Malfunctions which could impair safety should be rectified immediately.

#### **High Voltage**

Electrical cords must be properly laid and installed. The length and quality of the cords must be in accordance with local provisions.

Only qualified technicians may work on the electrical system. It is essential that the accident prevention regulations and those of the employers' liability associations are observed.

- Each time before starting up, make sure that the power supply agrees with the specifications of the product.
- Check the power cord for damage each time the site is changed. Damaged power cords should be replaced immediately and may never be reused.
- Check the leads for damage. Damaged leads should be replaced immediately and may never be reused.
- Do not try to insert anything sharp or metallic into the vents or the case.
- · Liquids may cause short circuits or other damage. Always keep the device and the power cords dry. Do not handle it with wet hands.

# Requirements for the Installation

Make sure that the device is not exposed to direct sunlight. Do not place anything on top of the device, and do not place it on top of another heat producing device, so that the air can circulate freely.

# Grounding

This product is grounded through the grounding conductor on the power cord. To avoid electric shock, the grounding conductor must be connected to earth.

# **Orient the Equipment Properly**

Do not orient the equipment so that it is difficult to manage the disconnection device.

# IMPORTANT SAFFTY ADVICE

# **High Voltage**

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Requirements for the Installation Make sure that the device is not exposed to direct sunlight. Do not place anything on top of the device, and do not place it on top of another heat producing device, so that the air can circulate freely.

# **Explanation of the Symbols used**



Caution / Warning

DC, direct current

#### **Guarantee and Liability**

The General conditions of sale and delivery of Multi Channel Systems MCS GmbH always apply. The operator will receive these no later than on conclusion of the contract.

Multi Channel Systems MCS GmbH makes no guarantee as to the accuracy of any and all tests and data generated by the use of the device or the software. It is up to the user to use good laboratory practice to establish the validity of his / her findings.

Guarantee and liability claims in the event of injury or material damage are excluded when they are the result of one of the following.

- → Improper use of the device.
- → Improper installation, commissioning, operation or maintenance of the device.
- → Operating the device when the safety and protective devices are defective and/or inoperable.
- Non-observance of the instructions in the manual with regard to transport, storage, installation, commissioning, operation or maintenance of the device.
- → Unauthorized structural alterations to the device.
- → Unauthorized modifications to the system settings.
- → Inadequate monitoring of device components subject to wear.
- → Improperly executed and unauthorized repairs.
- → Unauthorized opening of the device or its components.
- → Catastrophic events due to the effect of foreign bodies or acts of God.

# IMPORTANT SAFFTY ADVICE

# **Operator's Obligations**

The operator is obliged to allow only persons to work on the device, who

- → are familiar with the safety at work and accident prevention regulations and have been instructed how to use the device;
- → are professionally qualified or have specialist knowledge and training and have received instruction in the use of the device;
- → have read and understood the chapter on safety and the warning instructions in this manual and confirmed this with their signature.
- → It must be monitored at regular intervals that the operating personnel are working safely.

Personnel still undergoing training may only work on the device under the supervision of an experienced person.

## **System Requirements**

For the Multi Channel Suite software Microsoft Windows ®10, 8.1 (64 bit) operating systems is required. English and German versions supported. Other language versions may lead to software errors.

One of the following Microsoft Windows operating systems is required for MC\_Rack: Windows 10, 8.1 or 7 (32 or 64 bit), English and German versions supported. Other language versions may lead to software errors.

If no MEA2100-System is present, MC\_Rack opens in a simulation mode. A computer with low performance may lead to performance limits more often; therefore, MCS recommends an up-to-date computer optionally with a separate hard disk. Please note that there are sometimes hardware incompatibilities of the MEA2100-System and computer components; or that an inappropriate computer power supply may lead to artifact signals. Please contact your local retailer for more information on recommended computer hardware.

Important: You need to have installed the latest MEA2100-System driver to operate the MEA2100-System, which is automatically installed with the data acquisition software. The installation may be invalid if the MEA2100-System does not respond. Please contact Multi Channel Systems or your local retailer in this case.

# **Recommended BIOS settings**

Recommended operating system settings

The following automatic services of the Windows operating system interfere with the data storage on the hard disk and can lead to severe performance limits in the data acquisition software. These routines were designed for use on office computers but are not very useful for a data acquisition computer.

- → Turn off Screen Saver.
- → Turn off Manual management of automatic Windows Update.
- → Power Options: Power scheme: Never turn on system standby.
- → It is also not recommended to run any applications in the background when using the data acquisition software.
- → Be careful when using a Virus Scanner. These programs are known to disturb the software and even data loss may occur.

When using a MEA2100-System it is recommended to connect a high performance computer with a separate hard disk for program files and data storage. The provided possibility to use up to 256 channels with up to 50 kHz needs high memory capacity. Please remove data and defragment the hard disk regularly to ensure optimal performance.

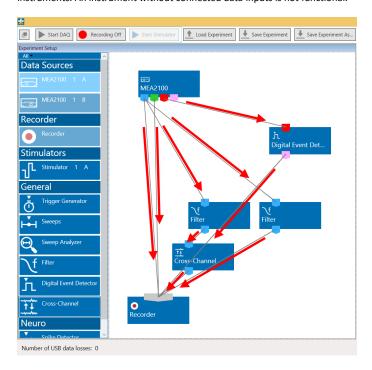
# **MULTI CHANNEL EXPERIMENTER SOFTWARE**

Please read the manual Multi Channel Experimenter for detailed information!

Please see the video Multi Channel Experimenter Overview for illustration.

#### **Building a Rack**

The "Multi Channel Experimenter" software operates with virtual instruments, which can be combined and saved as so called "Experiments" for later use. When opening the software, all available instruments are shown as blue icons on the left hand side of the screen. Each icon can be dragged and dropped in the main window. Most instruments have color coded data ports. Ports on the upper side represent data input to the instrument, ports on the lower side represent data outputs of the instrument. Only ports with matching colors can be connected by drawing a connection line between a data output and one or more data inputs. Data flows along those lines from the data source through the instruments. An instrument without connected data inputs is not functional.



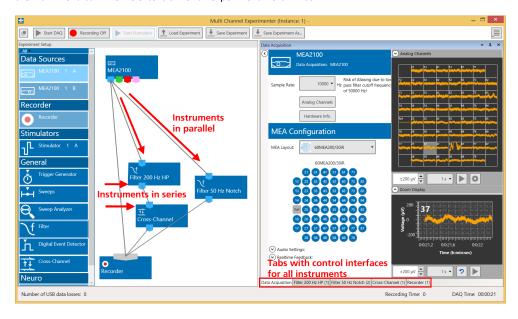
Clicking the button of any instrument with the right mouse provides three options: "Delete Instrument" for deleting the tool, "Edit Instrument Name" for changing the name and "Show Info" for information about the instrument. It is not possible to loop instruments.



Hovering the mouse pointer above an output port will give you a "Tooltip" with the data type the port provides. A right click on a data connection allows to delete the connection. A right click on an instrument brings up a menu which allows to delete or rename the instrument.

#### **Instrument Control Window**

A double click on each instrument opens a tab with the control interface for that instrument. Each instrument has its' own control window tab. The tab of the selected data source always shows the raw data. Most instruments can be selected more than once and be connected in parallel or in series. Exceptions are the data source, the recorder, and the stimulator, which can be selected only once. Once a configuration of instruments has been designed, it can be saved for later use. Such a configuration is called "Experiment", and can be saved and loaded from the main menu bar. The file extension for an experiment file is \*.mse.



The connecting lines between the instruments represent the flow of data. In the example above, there is a stream of raw data coming from the data source MEA2100 into the recorder directly and will consequently be recorded in the file. The same raw data stream is processed through a 200 Hz high pass filter, and the filtered data is further processed by the Cross-Channel Tool. The data processed by those two instruments is then connected to the recorder and will generate a second data stream with filtered AND referenced data in the recorded file. A third data stream will be the raw data filtered by a 50 Hz notch filter.

Instruments operate as independent units. They process the data from the respective input port and generate one or more data streams in the output port(s). Settings have to be done separately for each instrument in the respective control window tab.

# Multiple Data Sources, Multiple Software Instances



If multiple data sources are connected to the computer, they are indicated as separate icons in the Multi Channel Experimenter software. In case of a MEA2100-HS2x60, each individual MEA slot is a separate data source. Only one data source can be used in one instance of the software. Multiple instances can be opened simultaneously to control different data sources independently, for example two instances to control the two MEAs of a MEA2100-HS2x60. The active data source is shown in a light blue color. Data sources already occupied by another instance of the software are shown in grey. Not selected but available data sources are darker blue.

# **Data Types**

The types of output data occurring in the MEA2100-System, as indicated by the color-coded ports are:

Blue: Electrode data, raw or filtered, Cross-Channel data. These data types have the same structure and the same compatibility with instruments, hence they use the same data port color.

Green: Auxiliary analog data from the additional analog inputs on the Interface Board.

Red: Digital data, the 16 bit digital data stream from the Interface Board.

Pink: Trigger events.

#### File Types

The types of files generated with the Multi Channel Experimenter and the MEA2100-System are:

- \*.mse: Experiment file, a configuration of instruments. Created manually by the user.
- \*.msrd: Data file, generated by the Recorder, contains the raw data of all data streams.
- \*.msrs: Settings file, generated by the Recorder, must also be present to open a data file in the Multi Channel Analyzer.
- \*.html: Instrument settings, one \*.html file is generated by the Recorder with each data file. Each \*.html is linked to the \*.xml files of the individual instruments.
- \*. xml: One \*.xml per instrument is generated for each recording. It contains all settings of the respective instrument. Stimulation patterns in the Stimulator instrument can also be saved as \*.xml files by the user.

Please read the manual "Multi Channel Experimenter" for detailed information!

## MC\_Rack Software

Please read the MC Rack Manual for detailed information!

#### **Data Source Setup**

Every MEA headstage of the MEA2100-System can be operated completely independently by one instance of Multi Channel Experimenter or MC\_Rack data acquisition software. To be able to open more than one instance of MC\_Rack, please first open the "Advanced Configuration" dialog in the "Edit" menu.





Please increase the maximum number of instances according to the number of MEAs headstages you are going to use in parallel:

- → one MC\_Rack instance for one HS60 or one HS120,
- → two MC\_Rack instances for one HS2x60, or two HS60 or two HS120,
- → four MC Rack instances for two HS2x60.

Afterwards you can open several instances of MC Rack and assign every instance to one MEA headstage of the system.

After opening MC\_Rack as many times as necessary, please open the "Data Source Setup" dialog from the "Edit" menu. This dialog can only be opened in one instance at a time, please do the adjustments in one instance after the other. The example below shows the settings for one MEA2100-HS2x60.





Select "USB" and MEA2100 (S/N: XXXXX-A) as Data Source. Select "Configuration" in the "Source Layout". Please select the type of the connected headstage in the "Amp" drop down menu. If a MEA2100-HS2x60 is connected you have additionally to select the "Block" in the right drop down menu of "Virtual Device Configuration". For the first instance of MC\_Rack, select Block 1 (Channel 1...64) and for the second instance Block 2 (Channel 65...128). Select the appropriate MEA type from the drop down menu for each instance.

If a second headstage is connected to the same interface board, it will become available in the "Data Source Setup" as MEA2100 (S/N: XXXXX-B). The settings for the second headstage are analogous to the first.

#### Hardware Settings for the MEA2100-System in the Data Source

When using the MEA2100-System, the "Hardware" tab of the MC\_Rack software is modified. Please see also chapter "Defining a Data Source". In the "Hardware" tab of the Data Source, the gain setting must be adjusted to ensure a correct scaling of the data in MC\_Rack. The gain is a fixed hardware property, while sampling frequency and input voltage range of the data acquisition board can be selected according to the demands of the experiment.



The appropriate "Amplifier Gain" factor of 2 or 5, depending on the hardware, will automatically be entered. The "Input Voltage Range of Data Acquisition Board" divided by the gain is the "Signal Voltage Range", the maximum size of signals you can record before they get clipped. Please adjust the "Input Voltage Range of Data Acquisition Board" according to the expected size of your signals. It is advisable to select the input voltage range as small as possible, to ensure an optimal A/D resolution of the analog input signals. The "Sampling Frequency" should also be selected as low as possible, depending on the signals you like to measure, to minimize data file size. If several instances of MC\_Rack are used to operate the MEA2100-System, for example with a MEA2100-HS2x60 headstage or two MEA2100-HS120 headstages, each instance of MC\_Rack operates independently; you can define the "Input Voltage Range of Data Acquisition Board" and the "Sampling Frequency" for each instance of MC\_Rack individually.

# **Hardware Filter Settings**

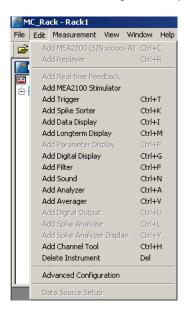
While the MEA2100-System in principle can measure DC signals, this is for most purposes very impractical, as the baseline would constantly drift. Therefore, the system is equipped with software configured hardware filters. By default, a second order high pass filter with a cut off frequency of 1 Hz is used to prevent a baseline drift. The upper cut off frequency is 3.3 kHz. It is possible to change the settings of these filters without modification of firmware or hardware. Please read chapter "MEA2100 Configuration Software". Additionally, you can use the software filters of MC\_Rack, if necessary.

# Setting up the Internal Stimulus Generator

The headstage of the MEA2100-System is equipped with an integrated 3-channel stimulus generator. The three stimulation channels operate independently. If two instances of MC\_Rack are used to operate two headstage, each MC\_Rack instance works completely independent, so three stimulation channels are available for each instance. If four instances of MC\_Rack are used to operate two headstages, for example MEA2100-HS2x60, each MC\_Rack instance works independent respectively, so twelve stimulation channels are available, three for each instance.

It is possible to choose between current or voltage controlled stimulation, and any electrode can be selected for stimulation. The control functions for electrode selection and definition of the stimulation parameters are integrated into MC\_Rack, you do not need any additional software. However, it is possible to import stimulation patterns generated in MC\_Stimulus II as ASCII data.

Add the internal stimulus generator to your rack: Click menu "Edit" and choose "Add MEA2100 Stimulator".



The following dialog appears.



Select the tab of any of the three stimulation channels (Stimulus 1, 2 or 3). In the "Stimulus" tab page, you can define the stimulation pulse and select how the stimulation is started and stopped.

Click "Stimulus 1" tab page, for example.



# Defining the stimulation pulse

In "Output Mode" you can choose whether you want to stimulate in voltage or current mode. To set up the stimulus pulse or pulse train, please use the eight provided up down boxes.



The individual stimulation pulse is defined in the "Pulse" window. Set up a monophasic pulse by selecting the voltage / current in mV/ $\mu$ A and the duration time T1 in  $\mu$ s. For setting up a biphasic pulse you have to select the stimulation strength and time also for the second phase. The shape of the pulse is displayed immediately in the window below. Once started, a programmed paradigm will run to its' end, or till it is manually terminated.



Warning: Anodic (positive) pulses can lead to a formation of titanium oxide on the MEA electrodes. When using MEA electrodes of TiN material, use only negative voltages pulses or biphasic current pulses applying the negative phase first. Always regard the safe-charge injection limits. Otherwise, electrodes can be irreversibly damaged by electrolysis.

When using the "Train" window for setting up a pulse train, please select the "Inter Pulse Interval IPI" in  $\mu$ s and the number of pulses in the train in "Repeat". If no pulse train is needed, set the IPI to zero and the Repeat to one.

The "Inter Train Interval ITI" function can be used to repeat a single pulse or a pulse train.

The interval time can be set in ms, and also the number of repeats. The complete programmed paradigm is shown in the graphical display below the stimulus window.

Once started, a programmed paradigm will run to its' end, or till it is manually terminated.

If the "Continuous Mode" is activated, the paradigm will be repeated indefinitely, till manually stopped. Please note that stimulation does not stop when MC Rack is stopped.



# Importing a stimulation file created with MC\_Stimulus II

To generate more complex stimulation patterns it is possible to import a stimulation file setup with the MC\_Stimulus II software as ASCII data. Please read the respective stimulus generator STG manual for detailed information about creating a stimulus file. You can import any pulse type available in MC\_Stimulus II.

Program the file in MC\_Stimulus II as usual: channel 1 will become stimulus 1 in MC\_Rack, channel 2 will become stimulus 2, and channel 3 will become stimulus 3.

Export the file as ASCII file (MC\_Stimulus II: File - Export ASCII)

Import this file in MC\_Rack (Stimulus Tab: Import File)

It is not necessary to program Sync Out pulses. Information in MC\_Stimulus Channel 4 and up and all Sync Out channels will be ignored.

The "Stimulus" interface will be disabled and the imported pattern will be shown in the graphical stimulus display. To skip the imported pattern and reactivate the "Stimulus" interface, click the "Unload File" button.



#### Starting and stopping the stimulation

In the "Trigger" drop down menu it is possible to choose different types of triggers to start the stimulation. The LED next to the Start / Stop button indicates the status of stimulation; the LED turns orange when the stimulation is running, the LED turns grey when the stimulation is stopped.

Important: It is **not** necessary for MC\_Rack to run in "Play" or "Record" mode to be able to start a stimulation paradigm, and a running paradigm will continue even after MC\_Rack is stopped. Once started, a programmed paradigm will run to its' end, or till it is manually terminated.



If "Manual" is selected in the "Trigger" drop down menu, the "Start" and "Stop" buttons can be used to control the stimulation manually.

If "Start" is selected, the stimulation starts as soon as MC\_Rack is started (in "Play" or "Record" mode). A delay between start of MC\_Rack and start of stimulation in ms can be selected in the "Pre" time window. You can stop the stimulation paradigm by pressing the "Stop" button.

If a "DigIn" is selected, the stimulation starts if a TTL pulse is delivered to the respective connectors Digital In 1 to 4 on the front of the MEA2100-Lite-System interface board.

If the internal STG is connected to one or more "Trigger Detectors" in the MC\_Rack virtual tree, it is also possible to start the stimulation on any of these Triggers (Trigger 1, 2 ...).

If the "Real-time Feedback" tool is activated, any of the internal STG can be started on one of the conditions defined in the Real-time Feedback tool (RF1, RF2, ...). Please see chapter "Real-time Feedback with MEA2100-System" for more information. The tool must be present and active, for the "Real-time Feedback" conditions to become available.

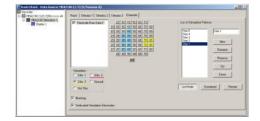
# Important: The Real-time Feedback is not available in MEA2100-Lite-Systems!

If a new trigger arrives before the programmed stimulation paradigm is finished, the paradigm starts again from the beginning. All three stimulus channels can be started and stopped independently.

To repeat a stimulation pulse in a loop, activate the "Continuous Mode". The pulse will be applied continuously until it is stopped by manually with the "Stop" button.

#### Selection of stimulation electrodes

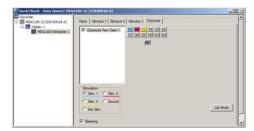
Click the "Channels" tab to assign the programmed stimulation patterns to individual electrodes, and to activate the blanking circuit BC, and to operate the "List Mode".



To apply the stimulation pattern of a specific stimulation channel (Stim. 1, 2 or 3) to one or more electrodes, select the desired stimulation channel (Stim. 1 to 3) and click the electrodes you want to apply this paradigm to. To apply the stimulation pattern to all electrodes, click the button "All" below the grid. Electrodes can be grounded or selected as regular recording electrodes (Not Stim.) in the same way.

Electrodes selected for stimulation pattern 1 "Stim.1" are colored in blue, for stimulation pattern 2 "Stim. 2" are colored in red, or stimulation pattern 3 "Stim. 3" are colored in yellow. To cancel a stimulation electrode, please use the radio button "Not Stim." and click on the selected electrode.

The blanking feature to avoid stimulation artifacts can be activated or deactivated via the check box "Blanking".



# Blanking

A blanking signal transiently switches off the input stage of the amplifier during the stimulus, thus avoiding stimulus artifacts on non-stimulating electrodes.

Amplifier saturation is effectively prevented, and the recovery time is greatly reduced. During the blanking period, a flat line is displayed. This blanking period extends a few hundred microseconds before and after the actual stimulus, currently  $600 \mu s$ , but might be subject to change. The pre- and post-time are experimentally optimized and cannot be changed by the user.

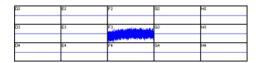
#### **Dedicated Stimulation Electrodes**

The function "Dedicated Stimulation Electrodes" can be used to further avoid stimulation artifacts on the electrodes surrounding the stimulation electrode, which are sometimes not completely removed by the blanking alone. Usually, the stimulation electrode will be connected to the stimulator output only during the stimulation pulse, and afterwards be switched back to the amplifier to be used as recording electrode. This sometimes causes switching artifacts independently from the actual stimulation.

However, if the function "Dedicated Stimulation Electrodes" is active, the selected stimulation electrodes will be constantly connected to the stimulator outputs. This causes permanent higher noise on the selected stimulation electrodes, and makes of course recording on the stimulation electrodes impossible, but almost completely removes residual artifacts. The images below show stimulation on electrode F3 with and without "Dedicated Stimulation Electrodes" activated.

Note: The artifact suppression additional to blanking via "Dedicated Stimulation Electrodes" is not available when using the "List Mode".

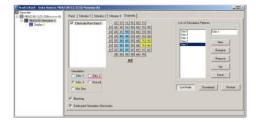
"Dedicated Stimulation Electrodes" selected (X-Axis: 1000 ms, Y-Axis: ± 500 μV)



"Dedicated Stimulation Electrodes" deselected (X-Axis: 1000 ms, Y-Axis:  $\pm$  500  $\mu$ V)

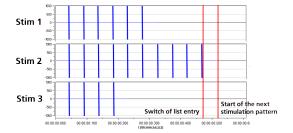
| D1 | E1 | F1 | G1 | н   |  |
|----|----|----|----|-----|--|
|    |    | 1  | 1  |     |  |
| D2 | E2 | F2 | GZ | H2  |  |
|    |    |    | -  |     |  |
| D3 | E3 | F3 | G3 | H3  |  |
|    |    |    |    |     |  |
| D4 | E4 | F4 | G4 | 114 |  |
|    |    |    |    |     |  |

# List Mode



Clicking the button List Mode opens an additional window: List of Stimulation Patterns. In List Mode it is possible to generate and download a list of up to 256 user defined stimulation patterns, which will then be applied automatically one after the other.

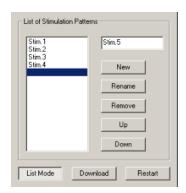
When the "List Mode" is activated, the three stimulator units are coupled to a single starting trigger. The starting trigger is set in the tab of the first stimulator unit, Stimulus 1. In Stimulus 2 and 3, the respective functions are disabled. To uncouple the stimulator units again, close the List Mode dialog. The step from one stimulation pattern to the next in the list happens when the start condition defined for Stimulus 1 occurs (for example, manual start, incoming trigger, real-time feedback trigger) and all three stimulator units are idle. Please see the red bars on the picture. However, the next pattern can only be started by the respective starting condition when the previous stimulation paradigm, including all breaks, is completely finished.



That means, if one stimulation pattern of any of the three stimulator units is still running when the condition occurs, nothing will happen. This also holds true when a stimulator unit is not actually used in the currently active stimulation pattern. Hence, the longest programmed stimulation pattern determines the minimum possible time between two starting triggers, even if the respective stimulator unit is not actually used. It is therefore advisable to set a stimulation pattern with a length of 0 on all unused stimulator units and keep all patterns as short as possible.

A stimulation pattern can contain single or multiple stimulation electrodes and may get an user defined name. To create a list of different stimulation patterns, please do the following.

Click the button "List Mode". There are two windows in the "List of Stimulus Pattern". The small window on the right side is for typing in a name for a pattern. In the window on the left side the list of stimulation pattern will be displayed and arranged.



When opening the "List Mode" for the first time, the term "New" appears and the current stimulation pattern is the first stimulation pattern in the list. To change the name, please overwrite the name with the specific name of this pattern in the small window.

To insert a stimulation pattern, select with the mouse the position in the list where you want to place the pattern. The line will be highlighted in blue. Type the specific name of this pattern in the small window. Click the button "New" and the new list entry appears.

To append a pattern, select the line under the last list entry. The line will be highlighted in blue. Type the specific name of this pattern in the small window. Click the button "New" and the new list entry appears.

To rename a pattern of the list, select the pattern which will be highlighted in blue. Then you can change the name of the pattern in the list. Please click the "Rename" button.

The command "Remove" eliminates the pattern in the list, which is highlighted in blue. With "Up" or "Down" you can move the patterns to arrange them in that sequence you like to apply them.

Click "Download" to download the list of stimulation patterns to the internal stimulus generator of the MEA2100 headstage.

To start the stimulation patterns in the list mode, please use the "Trigger Start" in "Stimulus 1" tab of this dialog. The trigger start in Stimulus 2 and Stimulus 3 tab will not be available, but all three triggers run simultaneously.

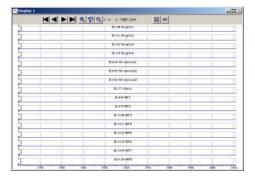
The stimulation patterns from the list will be applied one after the other and change every time the start condition defined for Stimulus 1 occurs and all three stimulator units are idle, as described above. When the end of the list is reached, the software jumps back to the first pattern and continues. When the "Restart" button is pressed, the software jumps to the first entry in the list, respectively.

# Use of the Digital Channel in the MEA2100-System

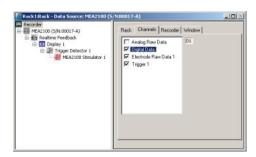
In contrast to the other MEA- and ME-Systems from Multi Channel Systems, the 16 input bits of the digital channel are not all accessible for external trigger signals but are mostly used for internal communication between the different components of the MEA2100-System. Only the first four bits are connected to the physical DigIn connectors on the front side of the MEA2100 interface board. Most bits are permanently assigned to certain functions. However, these settings can be customized if necessary. Please see the channel assignments from the following table.

| Bit 0  | DigIn 1    | Digital In channel 1               |
|--------|------------|------------------------------------|
| Bit 1  | DigIn 2    | Digital In channel 1               |
| Bit 2  | DigIn 3    | Digital In channel 1               |
| Bit 3  | DigIn 4    | Digital In channel 1               |
| Bit 4  | Stimulus 1 | Stimulation pattern on channel 1   |
| Bit 5  | Stimulus 2 | Stimulation pattern on channel 2   |
| Bit 6  | Stimulus 3 | Stimulation pattern on channel 3   |
| Bit 7  | Zero       | not connected                      |
| Bit 8  | RF 1       | Real-time feedback specification 1 |
| Bit 9  | RF 2       | Real-time feedback specification 2 |
| Bit 10 | RF 3       | Real-time feedback specification 3 |
| Bit 11 | RF 4       | Real-time feedback specification 4 |
| Bit 12 | RF 5       | Real-time feedback specification 5 |
| Bit 13 | RF 6       | Real-time feedback specification 6 |
| Bit 14 | RF 7       | Real-time feedback specification 7 |
| Bit 15 | RF 8       | Real-time feedback specification 8 |

To monitor the digital data stream, you can use the "Digital Display" tool. If a MEA2100 device is connected, the input bits will be labeled according to their function in the digital display.



To record the digital data stream in the data file, please enable the respective check box in the "Channels" tab of the Recorder tool.



# Triggering on Stimulation Pulses from Internal STGs

It is possible to trigger on stimulation pulses from any of the three internal stimulus generators. The three internal STG units send a trigger signals with each stimulation pulse on bits 4, 5 and 6 of the digital channels, Stimulus 1 on bit 4, Stimulus 2 on bit 5 and Stimulus 3 on bit 6. Please see chapter "Use of the Digital Channel in the MEA2100" for more details. So, to trigger, for example on each pulse of Stimulus 1, a Trigger detector in MC\_Rack must be set to the Digital Channel, bit 4. Please see screenshot below.



It is also possible to set the trigger detector to react on a signal from any of the three STG units. This might for example be useful to start a triggered recording if a stimulus is applied from any of the STG units. All three bits must be unmasked, and the bit value must be defined as > 0. See chapter "Triggering on TTL Pulses" for more information.



Triggered recording and any instrument which is below the Trigger Detector in the virtual tree of MC\_Rack can now work in relation to the selected STG unit(s).

#### Real-time Feedback with MEA2100-System

# Important: The Real-time Feedback is not available in MEA2100-Lite-Systems!

The interface board of the MEA2100-System is equipped with a high-capacity digital signal processor DSP. By moving the detection and analysis of signals from the data acquisition computer to the digital signal processor inside the interface, it is possible to run online filtering, analysis, and feedback stimulation in real-time. Please also read chapter "Real-time Feedback".

At the moment, the real-time feedback is available for one instance of MC\_Rack, which means for one MEA2100-HS60, one MEA2100-HS120, or one MEA of a MEA2100-HS2x60.

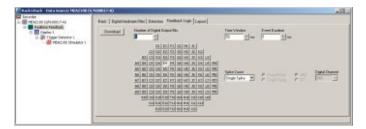
By default, eight of the 16 bits of the digital channels are permanently assigned to the "Real-time Feedback" function. For each of these eight bits, a different condition can be defined to release a trigger signal. These eight bits can be monitored with the Digital Display. See also "Use of the Digital Channel in the MEA2100". The "Real-time Feedback" trigger signals are available in the "Trigger Detector" and can also be directly selected to start the internal stimulus generators. See also chapter "Starting and Stopping the Stimulation".

To allow communication between different instances of MC\_Rack and different MEAs, respectively, the "Real-time Feedback" trigger signals are accessible in all MC\_Rack instances belonging to one MEA2100-System. Hence, it is possible to use signals detected on one MEA to control stimulation on a different MEA. This works if both MEAs are on the same headstage (HS-2x60), but also if they are on different headstages connected to the same interface board.

#### Setting up the Real-time Feedback Software

The "Real-time Feedback" works the same way as with the other data acquisition systems of Multi Channel Systems. The "Real-time Feedback" tool must be the first instrument under the data source. Click "Edit" menu and add "Real-time Feedback" or click the real-time feedback icon in the toolbar. Please also read the chapter "Real-time Feedback" in MC Rack manual for details.

However, the dialog of the "Feedback Logic" tab is different for MEA2100-Systems. While the user can freely assign up to 16 different detection conditions to the 16 bits of the Digital Out channel in the other MEA- and ME-Systems, the MEA2100 offers by default up to eight conditions permanently assigned to eight bits of the Digital Channel. See also "Use of the Digital Channel in the MEA2100".



# Synchronizing other instruments in with the internal stimulator

Most instruments usually used in combination with electrical stimulation need a trigger which marks the exact time point of the stimulation pulse, for example a triggered display or an "Analyzer". At the moment, the easiest way to achieve this is to use a "Trigger Detector" which controls the internal stimulator and also all following analysis instruments. If this "Trigger Detector" is then set to generate an "Automatic Trigger", it can be used to pace the complete instrument.

For example, if you want to apply a single biphasic stimulus to your MEA continuously every 10 s and analyze the resulting signals with an Analyzer tool, you could use a rack like this:



The internal stimulator is programmed to produce only a single voltage pulse on every trigger coming from "Trigger Detector Trigger 1". The "Trigger Detector" generates an "Automatic Trigger" continuously every 10 s.



The "Analyzer" and all other additional instruments can also operate on "Trigger 1" and are thereby synchronized with the stimulus pulse from the internal stimulator. The stimulation channels 2 and 3 could be started on the same trigger, or on different triggers.

#### **SETTING UP CARDIO 2D SOFTWARE**

When operating a MEA2100-System, you can connect the devices to any data acquisition computer. Make sure that the recommended system requirements are fulfilled.

The data acquisition computer from Multi Channel Systems MCS GmbH together with the MEA2100-System comes preinstalled and preconfigured for a flawless operation. You should contact your local retailer for assistance if you want to install additional hard- or software, or if you want to replace the computer, as incompatibilities of hardware components or software settings with the MEA2100-System or Cardio2D may occur.

Caution: You have acquired a high performance data acquisition and analysis computer. Do not modify the system, do not install new hard-or software, or another operating system without asking MCS or your local retailer for advice. Especially do not install virus scanners or firewalls because these programs are known to interfere with the data transfer to the hard disk. MCS cannot guarantee that a modified system is fully operational. Even data loss may occur.



Warning: The operating system settings of the data acquisition computer were preconfigured by MCS and should not be changed by the user. Changing these settings can lead to program instabilities and data loss.

Important: Please do not run MC\_Rack software program from Multi Channel Systems MCS GmbH in parallel to Cardio2D software!

Please check the system requirements before you install the software. MCS cannot guarantee that the software works properly if these requirements are not fulfilled.

Important: Please make sure that you have full control over your computer as an administrator. Otherwise, it is possible that the installed software does not work properly.

# Installing the Cardio2D Software

Make sure to have a valid license for the Cardio2D software! Please ask license@multichannelsystems.com.

You do not need a license for the Cardio2D software if you like to test the software for getting an idea of how it works and what is possible. You can test all functions, run the viability test to see your data, but you are not able to start an experiment.

Please contact license@multichannelsystems.com to receive a valid license key.

To enter the following dialog, select "License Key" in menu "Help". Please type the key into the window "Please enter license key" and confirm the key with "Set".



Double-click the Cardio2D.exe on the installation volume. The installation assistant will show up and guide you through the installation procedure. Follow the instructions of the installation assistant.

Note: The hardware driver is installed (or updated) automatically.

Note: If you connect, for example, two MEA2100 headstages via interface board to one data acquisition computer you need to have two license keys, for each MEA2100 headstage A and MEA2100 headstage B a separate key. But you do not need four licenses when using headstages with two MEA slots, for example MEA2100-HS2x60.

## Installing the Cardio2D+ Analyzer Software

Double-click the Cardio2D+.exe on the installation volume. The installation assistant will show up and guide you through the installation procedure. Follow the instructions of the installation assistant. You will again be asked for a path to put the log and data files. Cardio2D+ does not produce raw data files, result files only. Raw data files created by Cardio2D are never changed by Cardio2D+ but analyzed and saved as result files. It is advisable to use the same subfolders as used by the Cardio2D.

#### MEA2100 HARDWARE CONFIGURATION

The MEA2100-System is a flexible system, which can be used in different configurations. At the moment four types of headstages are available for the MEA2100-System, which can be connected to the interface board once or twice: A headstage for one MEA with 60 electrodes (MEA2100-HS60), with 120 electrodes (MEA2100-HS120) or with 256 electrodes (MEA2100-HS256).

Respectively a headstage for two MEAs is available, for two MEAs with 60 electrodes each (MEA2100-HS2x60). One or two of these types of headstages can be connected to the interface board of the MEA2100-System.



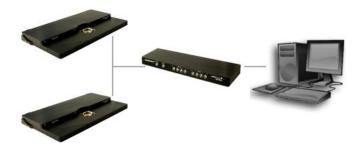
MEA2100-HS256



MEA2100-HS60 or MEA2100-HS120



Two MEA2100-HS2x60



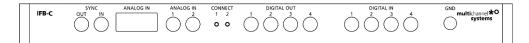
Two MEA2100-HS60 or two MEA2100-HS120

#### Interface Board IFB-C Multiboot



The Multiboot Interface Board IFB-C facilitates operation of all MCS *in vitro* and *in vivo* headstages within the entire 2100 amplifier solution suite. This suite includes: MEA2100-HS, Multiwell-MEA-HS, CMOS-MEA-HS, MEA2100-Beta-Screen-HS, W2100-HS and ME2100-HS. The modular 2100 amplifier solution suite design makes it easy to modify your lab equipment generally with modest hardware upgrade investments.

# **Front Panel**



From left to the right:

# Sync OUT / IN

Two or more interfaces boards IFB-C can be daisy-chained by use of the SYNC Out / SYNC In connectors. All daisy-chained interface boards run on the same clock – to allow perfectly synchronized recordings in large settings.

## **Analog Channels**

Up to eight Analog In channels are available via 10-pin connector. Please read chapter 10-Pin Connector for Analog IN in the Appendix for more information about the pin layout.

The additional analog inputs are intended for recording additional information from external devices, for example, for recording patch clamp in parallel to the MEA recording.

# Analog Channels 1 and 2

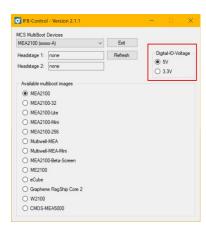
Two of these eight analog channels (Analog In No 1 and No 2) are separately available via Lemo connectors on the front panel of the interface board IFB-C.

#### **Two Status LEDs**

The status LEDs indicate the link status of the headstages HS 1 and / or HS 2. They light up when one or both headstage is connected to the IFB-C interface board via iX-industrial cable, type B.

# Digital IN / OUT

A Digital IN / OUT for 16 digital in- and output bits is available (Honda-PCS-XE68LFD) on the rear panel of the interface board. On the front panel four Digital IN and four Digital OUT bits are also accessible via Lemo connector (DIG IN bit 0 to bit 3 and DIG OUT bit 0 to bit 3). The Digital OUT delivers TTL pulses with 3.3 V or 5 V. The voltage can be switched between these two levels with the software IFB-Control, please read chapter "IFB-Control" in the Appendix.



If access to more bits of the DIG IN / OUT channel is required, it is necessary to connect a Digital IN / OUT extension Di/o board with a 68-pin standard cable. This Di/o board is available as an optional accessory.

#### Ground

If an additional ground connection is needed, you can connect this plug with an external ground using a standard common jack (4 mm).

# **Rear Panel**



From left to right:

# Toggle Switch On / Off

Toggle switch for turning the device on and off. The MEA2100-System is switched to status "ON" when the toggle switch is switched to the left. The device is switched "OFF" when the toggle switch is switched to the right. If the MEA2100-System is "ON", and the device is connected to the power line, the Power LED on the front panel of the interface board should light up. If not, please check the power source and cabling.

#### Power 24 VDC

Connect the power supply unit here. This power supply powers both, the interface board IFB-C and the headstage of the MEA2100-System. The device needs 24 V and 2.5 A / 60 W.

#### Ground

If an additional ground connection is needed, you can connect this plug with an external ground using a standard common jack (4 mm).

# Digital IN / OUT

A Digital IN / OUT for 16 digital in- and output bits is available via 68-pin Honda-PCS-XE68LFD connector. Please read chapter Digital IN / OUT Connector in the Appendix for more information about the pin layout of the connector. The Digital IN / OUT connection accepts or generates standard TTL signals. The Digital OUT delivers TTL pulses with 3.3 V or 5 V. The voltage can be switched between these two levels with the software IFB-Control, please read chapter "IFB-Control" in the Appendix.

TTL stands for Transistor-Transistor Logic. A TTL pulse is defined as a digital signal for communication between two devices. A voltage between 0 V and 0.8 V is considered as a logical state of 0 (LOW), and a voltage between 2 V and 5 V means 1 (HIGH).

The Digital OUT allows generating a digital signal with up to 16 bits and read it out, for example, by using a Digital IN / OUT extension Di/o board. You can utilize this digital signal to control and synchronize other devices with the MEA2100-System.

Bit 0 to 3 of the Digital OUT are separated and available as Lemo connector DIG OUT 0 to 3 on the front panel of the interface board. So, the Di/o extension is only necessary if more than four trigger inputs or outputs are needed.

The Digital IN can be used to record additional information from external devices as a 16 bit encoded number. The Digital IN is most often used to trigger recordings with a TTL signal. The 16 bit digital input channels is a stream of 16 bit values. The state of each bit (0 to 15) can be controlled separately. Standard TTL signals are accepted as input signals on the digital inputs.



Warning: A voltage that is higher than +3.3 Volts or +5 Volts or lower than 0 Volts, that is, a negative voltage, applied to the digital input would destroy the electronics. Make sure that you apply only TTL pulses (0 to 3.3 V or 5 V) to the digital inputs.

#### **Auxiliary Channels**

Two reserve auxiliary channels are available for future use. They have no function at the moment. It is possible to use them in conjunction with the Digital Signal Processor DSP for real-time feedback, please read chapter "Digital Signal Processor" below.

#### **Audio OUT**

To the Audio Out (3.5 mm phone jack) you can connect an audio system to make one or two of the electrode channels audible. This audio output is real-time. Headphones or speakers can be connected directly to the AUDIO OUT. Select the audible channels via software. Only two channels at a time can be converted into sound (Stereo).

# JTAG Connector

The JTAG connector has access to the digital signal processor DSP for real-time feedback. Please read chapter "Digital Signal Processor" below.

#### HS / SCU

Sockets for connecting up to two headstages via iX-industrial cable(s), type B.

# USB-C Connectors B and A

Both USB-C connectors are used to transfer the amplified and digitized data from all data channels and the additional digital and analog channels to any connected data acquisition computer via USB-C cable. Connector A corresponds with connector iX input 1, and connector B with iX input 2. If both iX inputs are used, also both USB-C connections must be used. Both USB cables must be connected to different USB-C ports of the computer, do not use an USB hub! Only use high grade USB-C cables, as provided with the MEA2100-System.

# **MEA2100 Headstages**

Amplifiers and the data acquisition for up to 252 channels and three independent stimulator units. The variable front part of the headstage contains the contact unit for different kinds of MEAs.

Headstage for microelectrode arrays (MEAs) with 256 electrodes.



Headstage for microelectrode arrays (MEAs) with 60 or 120 electrodes.



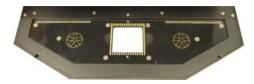
Headstage for two microelectrode arrays (MEAs) with 60 electrodes.



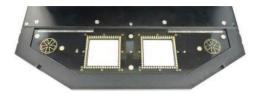
The rear part has connectors for the iX connector to connect the headstage to the interface board, and for the connection between the integrated heating element(s) of the headstage and the Temperature Controller TCO2 in the base plate. The contact unit houses the MEA(s) and features three grounding plugs for each MEA. These are internally interconnected and enable the user to ground an Ag/AgCl reference electrode or external components, like a perfusion system.

At the moment four different types of headstages are available for the MEA2100-System. They are designed for *in vitro* applications. Other variants of headstages, for example for *in vivo* application, are under development.

Headstage for microelectrode arrays (MEAs) with 60 electrodes.



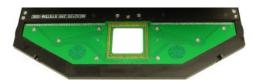
Headstage for two microelectrode arrays (MEAs) with 60 electrodes.



Headstage for microelectrode arrays (MEAs) with 120 electrodes.



Headstage for microelectrode arrays (MEAs) with 256 electrodes.



Additionally, the single or double headstages for 60 channels electrodes are also available with a modified ground plate to accommodate perforated MEAs. This feature needs to use perforated MEAs for perfusion from top and suction from the chamber below.

It is possible to connect two headstages to one interface and to control both headstages independently from each other by opening the data acquisition software Multi Channel Experimenter or MC\_Rack twice. A combination of two different headstages on one interface board is possible. In sum you can record from up to 240 electrodes.

The amplifiers and data acquisition integrated in the headstage support 120 electrode channels. The sampling rate, signal range and bandwidth can be adjusted via software control. Thereby the system is suitable for a broad range of applications, from single unit spike recordings to field potentials from whole heart preparations.

Electrode raw data acquired from the MEA chip is amplified and digitized by the analog / digital converter that is integrated in the headstage at sampling rates of up to 50 kHz per channel. Data is transferred to the interface board via iX-B cable.

A special advantage are the three integrated stimulus generator units, which deliver monophasic or biphasic rectangular pulses as single pulse and pulse trains. You can choose between current or voltage stimulation and you can select each MEA electrode for stimulation within Multi Channel Suite or MC\_Rack software. The integrated blanking circuit (BC) disconnects the electrodes from the amplifiers during the stimulation and avoids stimulus artifacts.

As usual in MEA-Systems, the MEA2100-System features a heating element with a Pt100 temperature sensor. If you connect a temperature controller TC02 to the heating element via D-Sub 9 connector, the heating element guarantees constant temperature conditions for the biological sample on the chip. A perfusion system with heating is available for the MEA2100 as optional accessory.

Because of the compact designed headstage you can use most inverted or upright microscopes, for the optical control of the sample on the MEA chip.

#### **Digital Signal Processor**

The IFB-C interface board of the MEA2100-System is equipped with a high-capacity digital signal processor DSP. The DSP allows online access to the data in real-time. Filtering, spike detection and generation of feedback stimulation can be controlled by the data acquisition software. Additionally, the processor is freely programmable to offer the advanced user more complex online analysis features. It can be programmed in C using the Code Composer Studio Development Environment from Texas Instruments. Simlink from Mathworks can also be used to create the model which will run on the DSP in the MEA2100.

The DSP has full access to the data stream from all electrodes in real-time and can analyze the data. It also can access the stimulation unit together with the blanking switches inside the stimulation unit of the MEA2100. This allows creating closed loop experiments with sub millisecond delays.

The processed data from the DSP can be streamed to the PC using a dedicated USB 3.0 connection.

#### **Bandwidth and Gain Specification**

The MEA2100 amplifier with blanking circuit is a 120-channel headstage with a hardware defined bandwidth. Default settings for the hardware filter will be 1 Hz to 3 kHz. However, a different bandwidth can be achieved by an additional software program, called "MEA2100 Configuration", no hardware modification is necessary. The hardware defined bandwidth marks the upper and lower limit of the frequency range, fine tuning within this range can be done with software filters. Please see the c for the "MEA Filter Configuration" software in the Appendix.

The MEA2100-System has a fixed hardware gain of 10. However, due to the large resolution of 24 bit, it is possible to adjust the actual signal input range used for recording in a wide range from  $\pm$  812  $\mu$ V to a maximum of  $\pm$  227 mV. The 24 bits are distributed among this complete voltage range.

In the MC\_Rack software, a window with 16 bit resolution can be adjusted on this range and display signals with high resolution in the following magnitudes:

 $\pm$  812  $\mu$ V;  $\pm$  1727  $\mu$ V,  $\pm$  3545  $\mu$ V;  $\pm$  7090  $\mu$ V;

± 14 mV; ± 28 mV, ± 57 mV; ± 114 mV; ± 227 mV

A smaller input range results in a better resolution in bits/ $\mu$ V, signals larger than the selected range will be clipped. In summary, the procedure has exactly the same functionality as a software selectable gain, even though, strictly speaking, it is not.

#### **DC Offset Correction**

The internal baseline restore routine is used to eliminate DC offsets of the electrode channels and set all baseline values to zero. This has to be a slow process. If the routine corrected too fast, slow signals would be eliminated as well.

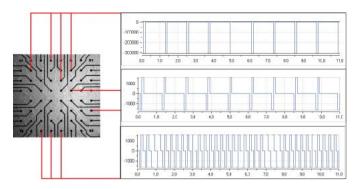
All electrodes on an array have different DC offsets at the beginning of an experiment. The DC offsets are amplified by the headstage, and the amplified output signal of the preamplifier is likely to exceed the input range of the filter amplifier. In order to eliminate this DC offset, a so-called baseline restorer is integrated in the headstage. For signals in the usual measurement range, the baseline restores routine acts like a high pass filter with a very low cut off frequency of roughly 0.01 Hz.

Due to the low cut off frequency, the baseline restorer takes some time to stabilize after switching on the amplifier or after replacing the MEA. One to two minutes are quite normal. During this time, the filter amplifier input will be overloaded, and you will see only a straight line with very low noise. This is considered a normal behavior and should not trouble you. Please wait until the baseline restore routine has been completed. After about one minute, the baseline restorer of the headstage has corrected the DC offset, and the output signals are now in the operating range of the filter amplifier. Now you should see a noise level of about 20 µV.

# **Stimulus Generator**

The headstage of the MEA2100-System is equipped with an integrated three channel stimulus generator, which delivers rectangular pulses in three different stimulation patterns: monophasic, biphasic and pulse trains. You can choose between current or voltage stimulation and you can select each electrode for stimulation. The integrated blanking circuit (BC) disconnect the electrodes from the amplifiers during the stimulation and avoids stimulus artifacts. Control of stimulation patterns and selection of stimulation electrodes is done within the data acquisition software.

Please read chapter "Setting up the Internal Stimulation Generator" for setting up and applying the stimulation parameters.



#### **SETTING UP THE MEA2100-SYSTEM**

#### **Connecting Headstages, Interface Board and Computer**

Provide a power supply in the immediate vicinity of the installation site.

→ Place all devices on a stable and dry surface, where the air can circulate freely and the devices are not exposed to direct sunlight.

Note: Take care that the headstage of the MEA2100-256-System will not overheat! Air condition is strongly recommended in the laboratory! Place the 256-channel headstage on thermoconducting material, metal for example, or put the headstage on stilts that the air can circulate freely!

Set up the computer (with installed data acquisition program).

- → Install the software from the installation volume if it is not already installed. The MEA2100-System is a plug and play device. The driver is automatically installed together with the data acquisition program.
- → Set up the MEA2100 headstage(s) on a microscope or on a solid table or workbench.
- → Connect the headstage/s via the provided iX, type B cable/s to the interface board IFB-C.
- → Connect the one or both USB 3.0 micro ports of the interface board to a free USB 3.0 port of the data proceeding acquisition computer. Do not use an USB hub and also avoid USB ports on the front panel of the computer, as they are often connected to the main board via an internal hub.
- → Connect the interface board via power supply unit to a power outlet of the same electrical system (connected to the same ground / earth wire) as all other components of the setup, for example, the computer or shielding.
- → If necessary, connect the system to an external ground.
- → Connect the internal heating element of the MEA2100 headstage to the temperature controller's output channel (D-Sub9 socket) with the provided cable. Do not connect the heating element cable to the computer!
- → Turn the toggle switch at the rear panel of the interface board on.
- Check the power LED. It should light up as soon as the power line is connected, and the toggle switch is switched on. If not, check the power source and cabling.
- → Start the data acquisition program and select the MEA2100-System as the data source.

Please see the Multi Channel Experimenter or MC\_Rack help or manual for more details on how to record and analyse data.

# Opening and Closing the Headstage

Open the lid of the headstage by pushing the two rectangular panels on the left and right side of the contact unit sideward. The upper part of the headstage swings open. The baseplate underneath the lid has either one or two slots for MEAs. Usually, each slot has a heating element with a hole in the middle to allow microscope access from the bottom. If equipped for perforated pMEAs, the heating element is replaced by a perfusion ground element with fluidic channels and an O-ring. Close the lid again by pushing the panels back in their original position.





#### **First functional Tests**

Each MEA2100-System has been thoroughly tested at the factory site before delivery. However, you may want to perform some tests yourself before you begin your experiment to exclude any damage that might have occurred during transportation, or to fulfill your own guidelines, for instance. Some of the tests will also help you to get to know the basic functions of the hard- and software, like a short tutorial. It will take only a few minutes time and can save time and trouble in the long run. Multi Channel Systems recommends running these tests after the setup of your system before you start your real experiments.

# **General Performance / Noise Level**



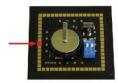
Please use the provided test model probe to test the amplifier immediately after installation. It simulates the behavior of a MEA electrode in a bath with conductive solution by a resistor of 220 kOhm and a 1 nF capacitor between ground and amplifier.

Test model probes are available for each type of headstage with respect to the number of electrodes on the MEA: Test60MEA, Test120MEA and Test256MEA.

Use Multi Channel Experimenter or MC\_Rack or your custom data acquisition program to record from the test model probe and to check the headstage. Please see the data sheet "Test Model Probe" in the Appendix. Alternative to the test model probe you can use a MEA Signal Generator.

A MEA Signal Generator is a convenient tool adapted for MEA2100-Systems with HS60 or HS2x60. Use the MEA-SG instead of setting up an experiment with biological sample for training, controlling, and troubleshooting purposes. This reduces the number of animal experiments and saves laboratory equipment. Please see the data sheet "MEA-SG" in the Appendix.

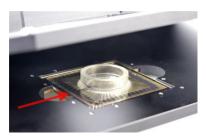
Important: When using a MEA-SG which is not adapted to MEA2100-System, the contact to the internal reference must be disconnected. Otherwise, the delivered signals are not acceptable. Please insert the MEA-SG in correct orientation as shown on the following picture. Cover the designated contact pad connected to the reference electrode, for example with isolation tape.



Signal generators are available for three types of headstages with respect to the number of electrodes on the MEA in use: 60MEA-SG, 120MEA-SG and 256MEA-SG.

#### **SETTING UP THE MEA**

Open the lid of the headstage. Place the MEA chip inside the MEA2100 headstage. The MEA is not rotationally symmetrical, so take care for the orientation of the MEA.



Important: MEAs are not symmetrical! That is, why the writing (for example NMI, LEITER, MEA type) on the MEA chip should be on the right side viewed from the front, when the headstage is open. MEAs with one big internal reference electrode should be placed with reference electrode to the left side in the headstage. Otherwise, the MEA layout will not match with the pin layout of the channel map in MC\_Rack.

You can use the engraved serial number as marker. The pin layout of the MEA is described in "MEA Datasheet" in the Appendix.



Warning: Spilled liquid can damage or even completely destroy the electronics of the MEA2100 headstage. Please be careful when setting up your perfusion system and when starting the perfusion. Take care that the flow rates of the inlet and outlet flow match so that flooding of the amplifier is efficiently prevented.

# **Grounding the Bath**

Most MEA chips are equipped with an internal reference electrode, which will be automatically connected to the systems ground when the MEA2100 headstage is closed. This has the advantage that you can keep the culture chamber closed and sterile (for example, with MEA-MEM semipermeable membranes).

If the MEA does not have an internal reference, please use the provided AgAgCl pellet or a silver wire to connect the bath to ground. The connectors beside the area for the MEA on the lid of the headstage are all internally connected to the system ground, so you can use any of them for grounding.

# **Temperature Controller TC02**



The MEA2100-System features a heating element with a PT100 temperature sensor. If you connect a temperature controller TC02 to the heating element via D-Sub 9 connector, the heating element guarantees constant temperature conditions for the biological sample, placed on the MEA.

# **Perfusion Cannula PH01**



When using a perfusion system, the perfusion cannula with heating element and sensor PH01 can be connected to a temperature controller TC02. This is very useful for general perfusion purposes, whenever the fluid stream needs to be temperature controlled. Magnetic holders for the PH01 and a suction cannula and a steel plate fitting the headstage of the MEA2100 are available as optional accessory.

For using pMEAs it is necessary to have a MEA2100-System equipped with a perfusion element. The perfusion element is available for headstages with one 60 electrode MEA and headstages with two 60 electrode MEAs. The perfusion element replaces the regular ground plate with heating element. It is possible to change exchange the one element for the other, but the exchange has to be done by MCS or a qualified distribution partner.

#### **Service and Maintenance**

You should clean the contact pins of the MEA2100 headstage carefully with a soft tissue and alcohol or isopropanol from time to time, especially if you have problems with the noise level. For handling and cleaning of the MEA, please refer to the MEA manual or to MEA Cleaning Quick Guide on the MCS web site www.multichannelsystems.com.



Warning: Please be very careful when handling the headstage or cleaning the device! The pins can be damaged easily.

#### **TROUBLESHOOTING**

The following hints are provided to solve problems that have been reported by users. Most problems occur seldom and only under specific circumstances. Please check the mentioned possible causes carefully when you have any trouble with the product. In most cases, it is only a minor problem that can be easily avoided or solved.

If the problem persists, please contact your local retailer. The highly qualified staff will be glad to help you. Please inform your local retailer as well, if other problems that are not mentioned in this documentation occur, even if you have solved the problem on your own. This helps other users, and it helps MCS to optimize the instrument and the documentation. Please pay attention to the safety and service information in the separate user manuals of the related products and in the software help. Multi Channel Systems has put all effort into making the product fully stable and reliable, but like all high-performance products, it has to be handled with care.

#### No Computer Connection / No Recording Possible

You cannot establish a connection to the computer. The MEA2100-System channel layout is not available in the data acquisition software. When loading a previously saved virtual rack file, you will get an error message and the simulator will be started automatically. You get an error message when starting the recording in MC\_Rack after a successful computer connection.

Possible causes:

? The power LED is not lightning. The supply power is not connected or there is a technical problem with the instrument.

Check the power source and the cable connections. If this does not solve the problem, contact your local retailer for support.

? The power LED is lighting. The USB port might not support USB 3.0 or might not be working.

Check the USB 3.0 port. Only high speed USB 3.0 ports can be used. Try another USB 3.0 port.

? You can establish a connection but get an error message when starting the recording in MC\_Rack. The bandwidth of the USB port is not sufficient for recording. This can be the case if the MEA2100-System is connected via USB hub, and a second device that sends or receives continuous data streams, for example, a web cam or USB speakers, is connected to the same USB port.

Connect the MEA2100-System directly to a USB 3.0 port, not via hub.

## Triggering / Digital Input does not Work

You have connected a TTL source to one of the digital inputs of the MEA2100-System and configured the virtual rack in MC\_Rack for triggering displays or data acquisition by the TTL source, but you do not see any sweeps.

Possible causes:

? The TTL source does not generate true TTL signals (> 1.5 to 5 V TTL level), or the TTL pulse duration is too short in combination with the sampling rate, so that the pulse is missed in-between two data points.

The MEA2100-System can only accept TTL signals as a digital input stream. The TTL pulse needs to be optimized according to the sampling rate. Otherwise, a detection of the trigger cannot be guaranteed.

? The software settings for the Trigger Detector do not match with the hardware configuration.

In MC\_Rack, add a Trigger Detector to your virtual rack, and select the Digital Data D1 input stream as the Trigger. Check the pin layout of the Digital IN / OUT connector and make sure that the same bit input that is connected is selected in the software. (The standard settings of the Trigger Detector are for using bit 0.) Mask all unused bits. Select the appropriate logical state (generally HIGH) for triggering. Please see the MC\_Rack help or manual for more details.

# **TROUBLESHOOTING**

#### **Noise on Single Electrodes**

The noise level on single electrodes is significantly higher than expected or you see artifact signals.

Possible causes:

? The electrode or the contact pin of the headstage may be defective. To test this, do the following.

Open the amplifier and turn the MEA by 90 degrees. Close the MEA2100 headstage again and start the recording.

If the same electrode in the MEA layout is affected, the amplifier's contact is not okay. If another electrode is now affected and the previously affected electrode is all right now, the MEA electrode is not okay, but the headstage is fine.

— OR —

Use the test model probe to test the MEA2100 headstage. If the noise level is fine without the MEA, bad MEA electrodes cannot be the cause.

#### MEA is defective

MEAs wear out after multiple uses or over a longer time of use, for example, for long-term cultures. This is considered a normal behavior. MEAs are also easily damaged by mishandling, for example, if wrong cleaning solutions or too severe cleaning methods are used or if the recording area is touched. If you observe a bad long-term performance of MEAs, consider a more careful handling.

Possible causes:

? The contact pads are contaminated.

Clean the contact pads carefully with a swab or a soft tissue and pure (100 %) alcohol.

? The contact pads or the electrodes are irreversibly damaged. You could have a look at the electrodes under a microscope: If they appear shiny golden, the TiN is gone, and the electrode is irreversibly damaged. Electrodes may be damaged without changing their visual appearance, though.

Pick one of the bad channels after the other and ground it. See the MEA amplifier's manual for more information on grounding channels. In most cases, only one of the electrodes that appear bad is actually defective, and the other ones are only affected by the single defective electrode. Ground as many electrodes as you need for a good general performance. Grounded electrodes show a noise level that is lower than that of good electrodes. If too many electrodes are defective, use a new MEA.

## Overall Noise / Unsteady Baseline

The baseline is unstable, signals are jumping or drifting.

Possible causes:

? Bath electrode is not connected to ground.

Check orientation of MEA with internal reference. The internal reference must be on the left side of the MEA when it is placed in the amplifier. If the MEA has an internal reference, use an Ag/AgCl bath electrode.

? AgCl bath electrode is not well-chlorided.

Rechloride the electrode or use a new one.

? 50 Hz hum: 50 Hz is the frequency of mains power in Europe. If the shielding and grounding of the setup is not sufficient, electrical signals are picked up from the environment.

Use a proper shielding. For example, you can place aluminum foil over and / or under the amplifier that is connected to the system ground (ground connectors of the headstage or ground connector in the back of the interface board). You can also use special shielding equipment like a Faraday cage.

#### Missing Spikes or Strange Signal Behavior

MEAs wear out after multiple uses or over a longer time of use, for example for long-term cultures. The insulation layer gets thin over time. This is considered a normal behavior.

Possible causes:

? The insulation layer is too thin. As a result, the MEA gets the behavior of a low pass filter. This means, that the signal frequency may be shifted to a lower frequency, and spikes are missing.

Optically control the MEA with a microscope. If concentric colored rings (Newton rings) are visible (due to light interference), the insulation layer is too thin and you should use a fresh MEA.

? The insulation layer has been abraded and is missing in parts. This will result in a short circuit between the electrodes or tracks and the bath. You will still see signals, but as an unspecific smear over the complete array.

Use a fresh MEA.

#### MCS FILTER CONFIGURATION SOFTWARE

The MCS Filter Configuration software is an add-on program for changing the hardware filter settings by the software. No firmware update is necessary. You can operate the software with MEA2100 (-Mini)-Systems and ME2100-Systems.

Please install the MCS Filter Configuration software by clicking the "McsFilterConfig.exe" file. Follow the installation guide as usual.

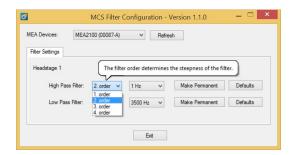
Main Window of the MEA Filter Configuration program:



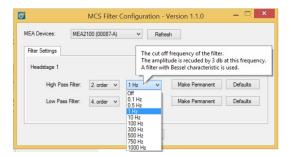
The MCS Filter Configuration program for changing the hardware filter setting of the MEA2100-System is self-explanatory via tool tips. It is possible to control each headstage separately.

Define the "MEA Devices" from the drop-down box if two headstages or headstages with two MEAs are available. Press "Refresh" button to update the settings. The actual settings for "High and Low Pass Filter" for the selected headstage are displayed. If the actual settings are not on the drop-down list, "Custom" will be displayed.

Select the order of the filter from the first drop-down box. The message "The filter order determines the steepness of the filter" is shown. The higher the order, the steeper the cut off.

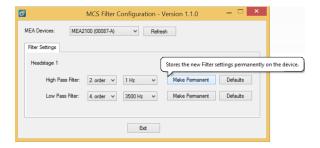


Select the cut off frequency of the filter from the second drop-down box. The message "The cut off frequency of the filter. The amplitude is reduced by 3 db at this frequency. A filter with Bessel characteristic is used." is shown.

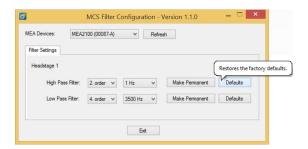


The option "Custom" cannot be selected. If you need a frequency which is not available on the list, please contact support@multichannelsystems.com.

The selected settings are automatically downloaded to the MEA2100 device as soon as you select them. If the "Make Permanent" button is not used, the device will be back to the last saved settings after a reset.

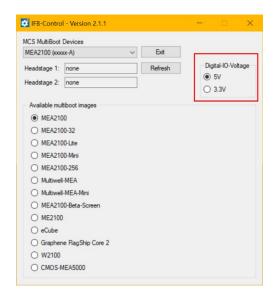


Click the button "Make Permanent" to store the selected filter settings permanently.



Click the button "Defaults" to refresh the factory default settings.

## IFB-CONTROL SOFTWARE



Software to control the MCS multiboot devices: Select the connected device and the headstages in the "MCS Multiboot Devices" window from the drop down menu.

Toggle between 5 V to 3.3 V in "Digital I/O Voltage".

Switch between system firmware available on the multiboot interface board IFB-C in "Available multiboot images" window.

#### **TECHNICAL SUPPORT**

Please read the chapter "Troubleshooting" of the manual first. Most problems are caused by minor handling errors. Contact your local retailer immediately if the cause of trouble remains unclear. Please understand that information on your hardware and software configuration is necessary to analyze and finally solve the problem you encounter. Please keep information on the following at hand:

Description of the error (the error message text or any other useful information) and of the context in which the error occurred. Try to remember all steps you had performed immediately before the error occurred. The more information on the actual situation you can provide, the easier it is to track the problem.

The serial number of the device. You will find it on the backside of the housing or click "About" in "Help" in the main menu of MC\_Rack.

The amplifier type and serial numbers of the connected amplifiers. You will find them on the devices.

The operating system and service pack number of the connected computer.

The hardware configuration (microprocessor, frequency, main memory, hard disk) of the connected computer. This information is especially important if you have modified the computer or installed new hard- or software recently.

The version of the recording software. On the "Help menu", click "About" to display the software version.

#### **TECHNICAL SPECIFICATIONS**

#### MEA2100-System



Warning: The device may only be used together with MEA chips from Multi Channel Systems MCS GmbH, and only for the specified purpose. Damage of the device and even fatal injuries can result from improper use. Do not open the headstage or the interface box and do not change hardware configuration as it could lead to improper behavior of the system.

#### **General characteristics**

Operating temperature 10 °C to 50 °C

Storage temperature  $0 \, ^{\circ}\text{C}$  to  $50 \, ^{\circ}\text{C}$ 

Relative humidity 10 % to 85 %, non-condensing

Headstage

Dimensions (W x D x H) 250 mm x 151 mm x 25 mm

Weight 1000 g

Type of headstage MEA2100-HS60 for 60-electrode MEAs

MEA2100-HS2x60 for 2 x 60-electrode MEAS MEA2100-HS120 for 120-electrode MEAs MEA2100-HS256 for 256-electrode MEAs

**Integrated Amplifier** 

Number of analog recording channels 60 to 256, depending on the headstage type

Data resolution 24 bit (16 bit if operated with MC\_Rack)

Signal input voltage range  $MC_{a}$ Rack: from  $\pm 4.9$  mV to  $\pm 500$  mV

Multi Channel Experimenter: ± 500 mV,

 $\pm\,250$  mV with MEA2100-HS256

Bandwidth 0.1 Hz to 10 kHz

Sampling frequency per channel up to 50 kHz, software controlled

Input impedance 1 G $\Omega$  || 10 pF, 450 M $\Omega$  || 18 pF with MEA2100-HS256

**Integrated Heating Element** 

Temperature sensor type Pt 100 with four wire connection, compatible with TC02

Accuracy ± 0.1 °C

# **TECHNICAL SPECIFICATION**

## **Integrated Stimulus Generators**

Output current  $\pm$  1.5 mA @  $\pm$  16 V compliance voltage

Output voltage  $\pm$  10 V @  $\pm$  20 mA max. compliance current

Stimulation pattern Multi Channel Experimenter: almost arbitrary patterns,

MC\_Rack: rectangle (biphasic, monophasic, pulse trains

Number of stimulation channels 3 independent stimulation patterns per 60 channels

2 independent stimulation patterns with MEA2100-HS256

Resolution 16 bit

Time resolution 20 μs

#### **IFB-C Multiboot Interface Board**

Dimensions (W x D x H) 250 mm x 83 mm x 25 mm

Weight 300 g

**Front Panel** 

2 Sync OUT and Sync IN Lemo connector, EPL.00.250 NTN

1 8-Channel Analog In 10-pin connector, DIL10Header-100mil

2 Analog Inputs, Channel 1 and Channel 2 Lemo connector, EPL.00.250 NTN

Signal input range for analog channels ± 10 V voltage input range @ 24 bit ADC

Gain for analog channels 2

2 LEDs LED light is on, while link to HS is working

4 Digital inputs Lemo connector, EPL.00.250 NTN

4 Digital outputs Lemo connector, EPL.00.250 NTN

1 Ground Common jack 4 mm, banana plug

**Rear Panel** 

I/O Switch On / Off

Power Supply MPU 30, PWR DC 0.65 x 2.75 mm

Ground Common jack 4 mm, banana plug

1 16 bit Digital In / Out 68-pin connector Honda-PCS-XE68LFD

2 Auxiliary channels (Not in use!)

# **TECHNICAL SPECIFICATION**

1 Audio Output Stereo jack 3.5 mm

1 Digital signal processor DSP 14-pin JTAG connector, DIL14Header-100mil-angeled

2 Interface board to headstage connectors iX- industrial, type B cable

2 USB-C ports USB-C cables

## Power supply unit (MPU 30)

Input voltage 110 - 240 V

Output voltage 24 V

Max. Power 65 W

Mark of conformity CE, TÜV, cUL

European standards EN60601

Software

Digital Signal Processor DSP TMS320C6454 ™ (Texas Instruments)

Operating system Microsoft Windows <sup>®</sup> 10, 8.1 (for Multi Channel Suite),

(32 or 64 bit), XP or Vista (for MC\_Rack) English and German version supported

Multi Channel Experimenter Version 2.17.4 and higher Multi Channel Analyzer Version 2.17.4 and higher MC\_Rack Version 2.9.3 and higher

Multi Channel DataManager Version 1.13.3 and higher MC\_DataTool Version 2.6.15 and higher

<sup>\*</sup> Important: In MC\_Rack software the scaling of the analog channels is not correct for a factor of 2, because the gain of the analog input channels is not considered.

## Pin Layout

#### Interface Board IFB-C

Pin Layout Interface Board (Rear Panel): Digital IN / OUT Connector

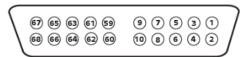


Interface Board (Front Panel): Separate Digital IN / OUT Lemo Connectors



Bit 0 to 3 of the Digital OUT are separated and available as Lemo connector DIG OUT 0 to 3 on the front panel of the interface board.

#### 68-Pin MCS Standard Connector (Honda-PCS-XE68LFD)



| Pin | 1       | GND                                   |
|-----|---------|---------------------------------------|
| Pin | 2       | GND                                   |
| Pin | 3 - 10  | Digital output channels bit 0 - 7     |
| Pin | 11 - 14 | GND                                   |
| Pin | 15 - 22 | Digital output channels bit 8 - 15    |
| Pin | 23 - 26 | GND                                   |
| Pin | 27 - 34 | Digital input channels bit 0 - 7      |
| Pin | 35 - 38 | GND                                   |
| Pin | 39 - 46 | Digital input channels bit 8 - 15     |
| Pin | 47 - 48 | GND                                   |
| Pin | 49 - 63 | Internal use (do not connect)         |
| Pin | 64 - 66 | GND                                   |
| Pin | 67      | Positive supply voltage output +3.3 V |
| Pin | 68      | GND                                   |

## Digital IN / OUT, separate available via Lemo Connectors

#### Separate Digital IN Lemo Connectors

Digital In 1 Bit 0 of the 16 bit digital input channels (Pin 27)

Digital IN 2 Bit 1 of the 16 bit digital input channels (Pin 28)

Digital IN 3 Bit 2 of the 16 bit digital input channels (Pin 29)

Digital IN 4 Bit 3 of the 16 bit digital input channels (Pin 30)

Separate Digital OUT Lemo Connectors

Digital OUT 1 Bit 0 of the 16 bit digital output channels (Pin 3)

Digital OUT 2 Bit 1 of the 16 bit digital output channels (Pin 4)

Digital OUT 3 Bit 2 of the 16 bit digital output channels (Pin 5)

Digital OUT 4 Bit 3 of the 16 bit digital output channels (Pin 6)

## Interface Board IFB-C: Analog IN (10-Pin Connector, DIL10Header-100mil)

Pin Layout Interface Board: Analog IN Connector



Two of the eight analog channels are additionally separate available via Lemo Connectors

Analog IN 1, Channel 1, Pin 3

Analog IN 2, Channel 2, Pin 4

The gain factor for amplification of all analog channels is 2.

## MEA2100 Interface Board: Analog IN (10-Pin Connector, DIL10Header-100mil)

97531 108642

Pin 1 GND

Pin 2 GND

Pin 3 Analog channel 1

Pin 4 Analog channel 2

Pin 5 Analog channel 3

Pin 6 Analog channel 4

Pin 7 Analog channel 5

Pin 8 Analog channel 6

Pin 9 Analog channel 7

Pin 10 Analog channel 8

## MEA2100 Interface Board: 14-Pin Connector JTAG for DSP (DIL14Header-100mil-angeled)





| Pin Number | 1   | 2    | 3   | 4   | 5   | 6     | 7     |
|------------|-----|------|-----|-----|-----|-------|-------|
| Assignment | TMS | TRST | TDI | GND | 3V3 | KEY   | TDO   |
|            |     |      |     |     |     |       |       |
| Pin Number | 8   | 9    | 10  | 11  | 12  | 13    | 14    |
| Assignment | GND | RTCK | GND | TCK | GND | EMU 0 | EMU 1 |

Input Connectors of the MEA2100-System from Contact Unit to Headstage

(100-Pin Fischer Connectors 50 mil)



Connector on the left side, when looking to the front of the MEA2100 headstage without contact unit and with the articulation of the headstage in the back.

Pin 1 and 2

Pin 3 to 30

Pin 31 to 34

Pin 35 to 38

Pin 39 to 98

Channel 1 to 60

Pin 99 and 100

GND (Ground)

Connector on the right side, when looking to the front of the MEA2100 headstage without contact unit and with the articulation of the headstage in the back.

Pin 1 and 2 GND (Ground)

Pin 3 and 62 Channel 61 to 120

Pin 63 to 66 GND (Ground)

Pin 67 to 70 internal coding

Pin 71 to 98 not connected

Pin 99 and 100 GND (Ground)

#### **CHANGING GOLD SPRING CONTACTS**

#### Instruction for the replacement of gold spring contacts inside the lid of the MEA2100 headstage.

Only experienced persons should replace the gold spring contacts, because they are small and lightweight buildings and can easily be destroyed!



Please follow the instructions with great care! Switch off the MEA2100 headstage and unplug the device from power supply.

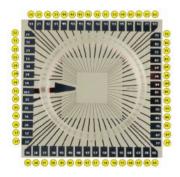
Define the pins which need to be changed with the software. Count the gold spring contacts in the lid of the amplifier to find the pin which need to be changed.

Please use the pin layout of a 120MEA200/30iR-Ti for the MEA2100-HS120, and the pin layout of a standard 60MEA200/30iR-Ti for the MEA2100-HS60 and MEA2100-HS2x60.

#### Pin Layout: Headstage HS60 or Headstage HS2x60

Please insert the 60MEA200/30iR-Ti as recommended. The internal reference electrode has to show to the left side, the writing "NMI MEA" to the right side when looking from the front of the headstage with the articulation in the back. Open data acquisition software, one instance for each MEA. Add the default map in the display and you find the designated pin layout. Count the pins to find the gold spring contact, you like to change.

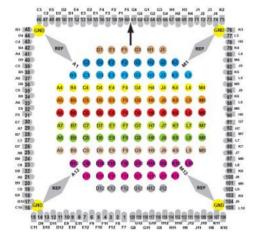
## Pin Layout of the 60MEA200/30iR-Ti



## Pin Layout: Headstage HS120

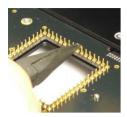
Please insert the 120MEA200/30iR-Ti as recommended. Use a binocular to control the position of the 120MEA. You can read the labeling of the electrodes A1 and M1, A12 and M12 in the edges of the electrode field, when looking from the front of the headstage with the articulation in the back. Open data acquisition software and add the default map for 120MEAs in the display and you find the designated pin layout. Count the pins to find the gold spring contact, you like to change.

## Pin Layout of the 120MEA200/30iR-Ti

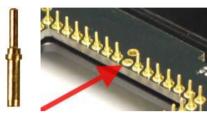


## **Changing Gold Spring Contacts in MEA2100 Headstages**

Open the MEA2100 headstage, turn it upside down to have a better access to the gold spring contacts in the lid. Place the device on a soft surface.



Grab the defective gold spring contact with a needle nose pliers and remove it upwards without damaging the contacts on the left and on the right

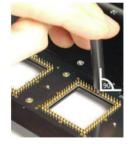


Place a new gold spring contact into the hollow shaft of the old one.

Take the fixing tool for gold spring contacts and put the small end of the tool over the head of the new gold spring contact straight from above.

Push the gold spring contact with the fixing tool into the shaft until the gold spring contact is engaged.



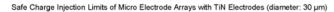


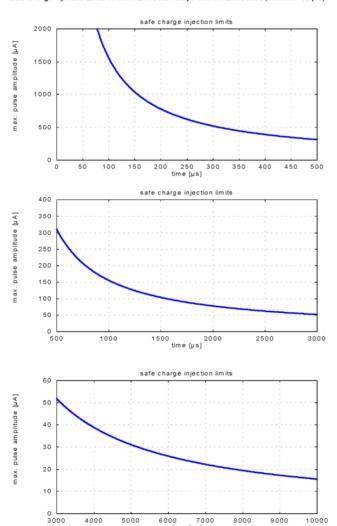
#### SAFE CHARGE INJECTION LIMITS

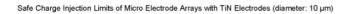
Titanium nitride (TiN) electrodes are generally more robust than electrodes from other materials, for example platinum (Pt). In the Appendix, you find safe charge injection limit curves that document maximum current and stimulus durations for standard TiN electrodes. Please note that these curves document the limits. Stimulus pulses should be kept safely below these limits. The safe charge injection limit of platinum (0.4 mC/cm²) is much smaller than for TiN (23 mC/cm²). This fact results in a considerably lower charge that you can inject into the electrode before faradic reactions occur that will lead to electrolysis of the electrode.

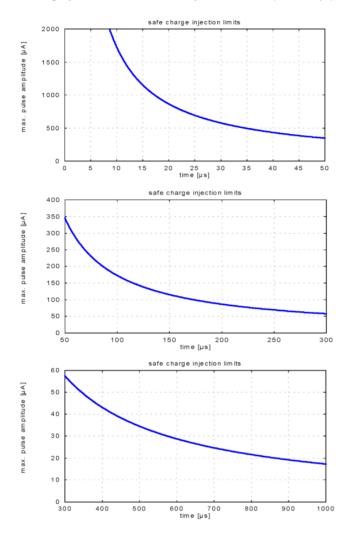
Please note that, when using voltage driven stimulation, the current flow to the electrode depends on the electrode impedance. The lower the impedance, the higher is the current. Please make sure to obey the safe charge injection limits always. Generally, TiN electrodes have lower impedances than Pt electrodes, and larger electrodes also have lower impedances than smaller.

When using TiN electrodes, it is extremely important to not charge the electrodes positively, as this will lead to electrolysis. This is not an issue for Pt electrodes. Therefore, when using voltage driven stimulation, it is important to apply negative voltages only. Positive voltages will shortly charge the electrodes positively, even though the electrode is discharged at the end of the pulse. As a consequence, biphasic voltage driven stimulation is not recommended. When using current stimulation, it is required to use biphasic stimulation, and to apply the negative phase first, to avoid a positive net charge on the electrode.









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